

## SEQUENCE LISTING

Lukyanov, Sergey
Lukyanov, Konstantin
Yanushevich, Yuriy
Savistky, Alexandr
Fradkov, Arcady

<120> Non Aggregating Fluorescent Proteins and Methods for Using the Same

```
<130> CLON-067
<140> 10/081,864
<141> 2002-02-20
<150> 10/006,922
<151> 2001-12-04
<150> 60/270,983
<151> 2001-02-21
<160> 30
<170> FastSEQ for Windows Version 4.0
<210> 1
<211> 687
<212> DNA
<213> Anemonia majano
<400> 1
atggctcttt caaacaagtt tatcggagat gacatgaaaa tgacctacca tatggatggc 60
tgtgtcaatg ggcattactt taccgtcaaa ggtgaaggca acgggaagcc atacgaaggg 120
acgcagacct cgacttttaa agtcaccatg gccaacggtg ggccccttgc attctccttt 180
gacatactat ctacagtgtt caagtatgga aatcgatgct ttactgcgta tcctaccagt 240
atgcccgact atttcaaaca agcatttcct gacggaatgt catatgaaag gacttttacc 300
tatgaagatg gaggagttgc tacagccagt tgggaaataa gccttaaagg caactgcttt 360
gagcacaaat ccacgtttca tggagtgaac tttcctgctg atggacctgt gatggcgaag 420
atgacaactg gttgggaccc atcttttgag aaaatgactg tctgcgatgg aatattgaag 480
ggtgatgtca ccgcgttcct catgctgcaa ggaggtggca attacagatg ccaattccac 540
acttcttaca agacaaaaaa accggtgacg atgccaccaa accatgcggt ggaacatcgc 600
attgcgagga ccgaccttga caaaggtggc aacagtgttc agctgacgga gcacgctgtt 660
gcacatataa cctctgttgt ccctttc
                                                                   687
<210> 2
<211> 229
<212> PRT
<213> Anemonia majano
```

```
<400> 2
Met Ala Leu Ser Asn Lys Phe Ile Gly Asp Asp Met Lys Met Thr Tyr
His Met Asp Gly Cys Val Asn Gly His Tyr Phe Thr Val Lys Gly Glu
                                25
Gly Asn Gly Lys Pro Tyr Glu Gly Thr Gln Thr Ser Thr Phe Lys Val
                            40
                                                45
Thr Met Ala Asn Gly Gly Pro Leu Ala Phe Ser Phe Asp Ile Leu Ser
Thr Val Phe Lys Tyr Gly Asn Arg Cys Phe Thr Ala Tyr Pro Thr Ser
                    70
                                        75
Met Pro Asp Tyr Phe Lys Gln Ala Phe Pro Asp Gly Met Ser Tyr Glu
                                    90
Arg Thr Phe Thr Tyr Glu Asp Gly Gly Val Ala Thr Ala Ser Trp Glu
            100
                                105
Ile Ser Leu Lys Gly Asn Cys Phe Glu His Lys Ser Thr Phe His Gly
                            120
                                                125
Val Asn Phe Pro Ala Asp Gly Pro Val Met Ala Lys Met Thr Thr Gly
                        135
                                            140
Trp Asp Pro Ser Phe Glu Lys Met Thr Val Cys Asp Gly Ile Leu Lys
                    150
                                        155
Gly Asp Val Thr Ala Phe Leu Met Leu Gln Gly Gly Asn Tyr Arg
                                    170
                165
Cys Gln Phe His Thr Ser Tyr Lys Thr Lys Lys Pro Val Thr Met Pro
                                185
Pro Asn His Ala Val Glu His Arg Ile Ala Arg Thr Asp Leu Asp Lys
                            200
                                                205
Gly Gly Asn Ser Val Gln Leu Thr Glu His Ala Val Ala His Ile Thr
                        215
                                            220
Ser Val Val Pro Phe
225
<210> 3
<211> 693
<212> DNA
<213> Zoanthus sp.
<400> 3
atggeteagt caaageacgg tetaacaaaa gaaatgacaa tgaaataccg tatggaaggg 60
tgcgtcgatg gacataaatt tgtgatcacg ggagagggca ttggatatcc gttcaaaggg 120
aaacaggcta ttaatctgtg tgtggtcgaa ggtggaccat tgccatttgc cgaagacata 180
ttgtcagctg cctttatgta cggaaacagg gttttcactg aatatcctca agacatagct 240
gactatttca agaactegtg teetgetggt tatacatggg acaggtettt tetetttgag 300
gatggagcag tttgcatatg taatgcagat ataacagtga gtgttgaaga aaactgcatg 360
tatcatgagt ccaaatttta tggagtgaat tttcctgctg atggacctgt gatgaaaaag 420
atgacagata actgggagcc atcctgcgag aagatcatac cagtacctaa gcaggggata 480
ttgaaagggg atgtctccat gtacctcctt ctgaaggatg gtgggcgttt acggtgccaa 540
ttcgacacag tttacaaagc aaagtctgtg ccaagaaaga tgccggactg gcacttcatc 600
cagcataagc tcacccgtga agaccgcagc gatgctaaga atcagaaatg gcatctgaca 660
```

gaacatgeta ttgcateegg atetgeattg ecc

```
<211> 231
 <212> PRT
 <213> Zoanthus sp.
 <400> 4
 Met Ala Gln Ser Lys His Gly Leu Thr Lys Glu Met Thr Met Lys Tyr
 Arg Met Glu Gly Cys Val Asp Gly His Lys Phe Val Ile Thr Gly Glu
 Gly Ile Gly Tyr Pro Phe Lys Gly Lys Gln Ala Ile Asn Leu Cys Val
 Val Glu Gly Gly Pro Leu Pro Phe Ala Glu Asp Ile Leu Ser Ala Ala
                         55
 Phe Asn Tyr Gly Asn Arg Val Phe Thr Glu Tyr Pro Gln Asp Ile Ala
                     70
Asp Tyr Phe Lys Asn Ser Cys Pro Ala Gly Tyr Thr Trp Asp Arg Ser
Phe Leu Phe Glu Asp Gly Ala Val Cys Ile Cys Asn Ala Asp Ile Thr
             100
                                 105
Val Ser Val Glu Glu Asn Cys Met Tyr His Glu Ser Lys Phe Tyr Gly
                             120
                                                 125
Val Asn Phe Pro Ala Asp Gly Pro Val Met Lys Lys Met Thr Asp Asn
                         135
Trp Glu Pro Ser Cys Glu Lys Ile Ile Pro Val Pro Lys Gln Gly Ile
                                         155
Leu Lys Gly Asp Val Ser Met Tyr Leu Leu Leu Lys Asp Gly Gly Arg
                                     170
Leu Arg Cys Gln Phe Asp Thr Val Tyr Lys Ala Lys Ser Val Pro Arg
                                 185
Lys Met Pro Asp Trp His Phe Ile Gln His Lys Leu Thr Arg Glu Asp
Arg Ser Asp Ala Lys Asn Gln Lys Trp His Leu Thr Glu His Ala Ile
                                             220
Ala Ser Gly Ser Ala Leu Pro
225
<210> 5
<211> 865
<212> DNA
<213> Zoanthus sp.
<400> 5
gagttgagtt tctcgacttc agttgtatca attttggggc atcaagcgat ctattttcaa 60
catggctcat tcaaagcacg gtctaaaaga agaaatgaca atgaaatacc acatggaagg 120
gtgcgtcaac ggacataaat ttgtgatcac gggcgaaggc attggatatc cgttcaaagg 180
gaaacagact attaatctgt gtgtgatcga agggggacca ttgccatttt ccgaagacat 240
attgtcagct ggctttaagt acggagacag gattttcact gaatatcctc aagacatagt 300
agactatttc aagaactcgt gtcctgctgg atatacatgg ggcaggtctt ttctctttga 360
ggatggagca gtctgcatat gcaatgtaga tataacagtg agtgtcaaag aaaactgcat 420
```

<210> 4

```
ttatcataag agcatattta atggaatgaa ttttcctgct gatggacctg tgatgaaaaa 480
gatgacaact aactgggaag catcctgcga gaagatcatg ccagtaccta agcaggggat 540
actgaaaggg gatgtctcca tgtacctcct tctgaaggat ggtgggcgtt accggtgcca 600
gttcgacaca gtttacaaag caaagtctgt gccaagtaag atgccggagt ggcacttcat 660
ccagcataag ctcctccgtg aagaccgcag cgatgctaag aatcagaagt ggcagctgac 720
agagcatgct attgcattcc cttctgcctt ggcctgataa gaatgtagtt ccaacatttt 780
aatgcatgtg cttgtcaatt attctgataa aaatgtagtt gagttgaaaa cagacaagta 840
caaataaagc acatgtaaat cgtct
<210> 6
<211> 230
<212> PRT
<213> Zoanthus sp.
<400> 6
Met Ala His Ser Lys His Gly Leu Lys Glu Glu Met Thr Met Lys Tyr
His Met Glu Gly Cys Val Asn Gly His Lys Phe Val Ile Thr Gly Glu
                                25
Gly Ile Gly Tyr Pro Phe Lys Gly Lys Gln Thr Ile Asn Leu Cys Val
                            40
Ile Glu Gly Gly Pro Leu Pro Phe Ser Glu Asp Ile Leu Ser Ala Gly
                        55
Phe Lys Tyr Gly Asp Arg Ile Phe Thr Glu Tyr Pro Gln Asp Ile Val
                    70
Asp Tyr Phe Lys Asn Ser Cys Pro Ala Gly Tyr Thr Trp Gly Ser Phe
Leu Phe Glu Asp Gly Ala Val Cys Ile Cys Asn Val Asp Ile Thr Val
                                105
Ser Val Lys Glu Asn Cys Ile Tyr His Lys Ser Ile Phe Asn Gly Met
                            120
Asn Phe Pro Ala Asp Gly Pro Val Met Lys Lys Met Thr Thr Asn Trp
                                             140
Glu Ala Ser Cys Glu Lys Ile Met Pro Val Pro Lys Gln Gly Ile Leu
                                        155
Lys Gly Asp Val Ser Met Tyr Leu Leu Leu Lys Asp Gly Gly Arg Tyr
                165
                                    170
Arg Cys Gln Phe Asp Thr Val Tyr Lys Ala Lys Ser Val Pro Ser Lys
                                185
Met Pro Glu Trp His Phe Ile Gln His Lys Leu Leu Arg Glu Asp Arg
                            200
                                                205
Ser Asp Ala Lys Asn Gln Lys Trp Gln Leu Thr Glu His Ala Ile Ala
                        215
                                            220
Phe Pro Ser Ala Leu Ala
225
                    230
<210> 7
<211> 678
<212> DNA
```

<213> Discosoma sp

```
<400> 7
atgcgctcct ccaagaacgt catcaaggag ttcatgcgct tcaaggtgcg catggagggc 60
acceptgaacg gccacgagtt cgagatcgag ggcgagggcg agggccgccc ctacgagggc 120
cacaacaccg tgaagctgaa ggtgaccaag ggcggccccc tgcccttcgc ctgggacatc 180
ctgtcccccc agttccagta cggctccaag gtgtacgtga agcaccccgc cgacatcccc 240
gactacaaga agctgtcctt ccccgagggc ttcaagtggg agcgcgtgat gaacttcgag 300
gacggcggcg tggtgaccgt gacccaggac tcctccctgc aggacggctg cttcatctac 360
aaggtgaagt tcatcggcgt gaacttcccc tccgacggcc ccgtgatgca gaagaagacc 420
atgggctggg aggcctccac cgagcgcctg tacccccgcg acggcgtgct gaagggcgag 480
atccacaagg ccctgaagct gaaggacggc ggccactacc tggtggagtt caagtccatc 540
tacatggcca agaagcccgt gcagctgccc ggctactact acgtggactc caagctggac 600
atcacctccc acaacgagga ctacaccatc gtggagcagt acgagcgcac cgagggccgc 660
caccacctgt tcctgtaa
<210> 8
<211> 225
<212> PRT
<213> Discosoma sp.
<400> 8
Met Arg Ser Ser Lys Asn Val Ile Lys Glu Phe Met Arg Phe Lys Val
                                     10
Arg Met Glu Gly Thr Val Asn Gly His Glu Phe Glu Ile Glu Gly Glu
            20
                                25
Gly Glu Gly Arg Pro Tyr Glu Gly His Asn Thr Val Lys Leu Lys Val
Thr Lys Gly Gly Pro Leu Pro Phe Ala Trp Asp Ile Leu Ser Pro Gln
                        55
Phe Gln Tyr Gly Ser Lys Val Tyr Val Lys His Pro Ala Asp Ile Pro
                                         75
Asp Tyr Lys Lys Leu Ser Phe Pro Glu Gly Phe Lys Trp Glu Arg Val
                85
Met Asn Phe Glu Asp Gly Gly Val Val Thr Val Thr Gln Asp Ser Ser
                                105
Leu Gln Asp Gly Cys Phe Ile Tyr Lys Val Lys Phe Ile Gly Val Asn
                            120
                                                 125
Phe Pro Ser Asp Gly Pro Val Met Gln Lys Lys Thr Met Gly Trp Glu
                        135
                                             140
Ala Ser Thr Glu Arg Leu Tyr Pro Arg Asp Gly Val Leu Lys Gly Glu
                                        155
Ile His Lys Ala Leu Lys Leu Lys Asp Gly Gly His Tyr Leu Val Glu
                165
                                    170
Phe Lys Ser Ile Tyr Met Ala Lys Lys Pro Val Gln Leu Pro Gly Tyr
                                185
Tyr Tyr Val Asp Ser Lys Leu Asp Ile Thr Ser His Asn Glu Asp Tyr
                            200
Thr Ile Val Glu Gln Tyr Glu Arg Thr Glu Gly Arg His His Leu Phe
    210
                        215
                                            220
Leu
```

```
<210> 9
<211> 696
<212> DNA
<213> Anemonia sulcata
<400> 9
atggcttcct ttttaaagaa gactatgccc tttaagacga ccattgaagg gacggttaat 60
gqccactact tcaagtgtac aggaaaagga gagggcaacc catttgaggg tacgcaggaa 120
atgaagatag aggtcatcga aggaggtcca ttgccatttg ccttccacat tttgtcaacg 180
agttgtatgt acggtagtaa ggccttcatc aagtatgtgt caggaattcc tgactacttc 240
aagcagtett teeetgaagg ttttaettgg gaaagaacca caacctaega ggatggagge 300
tttcttacag ctcatcagga cacaagccta gatggagatt gcctcqttta caaqqtcaaq 360
attettggta ataattttee tgetgatgge eeegtgatge agaacaaage aggaagatgg 420
gagccatcca ccgagatagt ttatgaagtt gacggtgtcc tgcgtggaca gtctttgatg 480
gecettaagt gecetggtgg tegteatetg aettgecate tecataetae ttacaggtee 540
aaaaaaccag ctgctgcctt gaagatgcca ggatttcatt ttqaaqatca tcgcatcgag 600
ataatggagg aagttgagaa aggcaagtgc tataaacagt acgaagcagc agtgggcagg 660
tactgtgatg ctgctccatc caagcttgga cataac
<210> 10
<211> 232
<212> PRT
<213> Anemonia sulcata
<400> 10
Met Ala Ser Phe Leu Lys Lys Thr Met Pro Phe Lys Thr Thr Ile Glu
 1
                 5
                                  . 10
Gly Thr Val Asn Gly His Tyr Phe Lys Cys Thr Gly Lys Gly Glu Gly
Asn Pro Phe Glu Gly Thr Gln Glu Met Lys Ile Glu Val Ile Glu Gly
                            40
Gly Pro Leu Pro Phe Ala Phe His Ile Leu Ser Thr Ser Cys Met Tyr
Gly Ser Lys Thr Phe Ile Lys Tyr Val Ser Gly Ile Pro Asp Tyr Phe
                    70
                                        75
Lys Gln Ser Phe Pro Glu Gly Phe Thr Trp Glu Arg Thr Thr Tyr
Glu Asp Gly Gly Phe Leu Thr Ala His Gln Asp Thr Ser Leu Asp Gly
Asp Cys Leu Val Tyr Lys Val Lys Ile Leu Gly Asn Asn Phe Pro Ala
                            120
                                                125
Asp Gly Pro Val Met Gln Asn Lys Ala Gly Arg Trp Glu Pro Ala Thr
                        135
                                            140
Glu Ile Val Tyr Glu Val Asp Gly Val Leu Arg Gly Gln Ser Leu Met
                    150
                                        155
Ala Leu Lys Cys Pro Gly Gly Arg His Leu Thr Cys His Leu His Thr
Thr Tyr Arg Ser Lys Lys Pro Ala Ala Leu Lys Met Pro Gly Phe
                                185
```

His Phe Glu Asp His Arg Ile Glu Ile Met Glu Glu Val Glu Lys Gly

200

```
Lys Cys Tyr Lys Gln Tyr Glu Ala Ala Val Gly Arg Tyr Cys Asp Ala
                         215
                                             220
Ala Pro Ser Lys Leu Gly His Asn
225
                    230
<210> 11
<211> 678
<212> DNA
<213> Artificial Sequence
<220>
<223> hybrid coding sequence
<400> 11
atgagetgea geaagaaegt gateaaggag tteatgeggt teaaggtgeg gatggaggge 60
accgtgaacg gccacgagtt cgagatcaag ggcgagggcg agggccggcc ctacgagggc 120
cactgcagcg tgaagctcat ggtgaccaag ggcggcccc tccccttcgc cttcgacatc 180
ctcagccccc agttccagta cggcagcaag gtgtacgtga agcaccccgc cgacatcccc 240
gactacaaga ageteagett eecegaggge tteaagtggg agegggtgat gaacttegag 300
gacggcggcg tggtgaccgt gagccaggac agcagcctca aggacggctg cttcatctac 360
gaggtgaagt tcatcggcgt gaacttcccc agcgacqqcc ccqtqatqca qcqqcqqacc 420
cggggctggg aggccagcag cgagcggctc tacccccggg acggcgtgct caagggcgac 480
atccacatgg ccctccggct cgagggcggc ggccactacc tcgtggagtt caagagcatc 540
tacatggcca agaagcccgt gcagctcccc ggctactact acgtggacag caagctcgac 600
atcaccagec acaacgagga ctacaccatc gtggagcagt acgagcggac cgagggccgg 660
caccacctct tcctctqa
                                                                   678
<210> 12
<211> 225
<212> PRT
<213> Artificial Sequence
<220>
<223> hybrid protein
<400> 12
Met Ser Cys Ser Lys Asn Val Ile Lys Glu Phe Met Arg Phe Lys Val
                 5
Arg Met Glu Gly Thr Val Asn Gly His Glu Phe Glu Ile Lys Gly Glu
Gly Glu Gly Arg Pro Tyr Glu Gly His Cys Ser Val Lys Leu Met Val
                            40
                                                45
Thr Lys Gly Gly Pro Leu Pro Phe Ala Phe Asp Ile Leu Ser Pro Gln
                        55
                                            60
Phe Gln Tyr Gly Ser Lys Val Tyr Val Lys His Pro Ala Asp Ile Pro
Asp Tyr Lys Lys Leu Ser Phe Pro Glu Gly Phe Lys Trp Glu Arg Val
                                    90
Met Asn Phe Glu Asp Gly Gly Val Val Thr Val Ser Gln Asp Ser Ser
```

105

```
Leu Lys Asp Gly Cys Phe Ile Tyr Glu Val Lys Phe Ile Gly Val Asn
                            120
Phe Pro Ser Asp Gly Pro Val Met Gln Arg Arg Thr Arg Gly Trp Glu
                        135
Ala Ser Ser Glu Arg Leu Tyr Pro Arg Asp Gly Val Leu Lys Gly Asp
145
                    150
                                         155
                                                             160
Ile His Met Ala Leu Arg Leu Glu Gly Gly His Tyr Leu Val Glu
                                    170
                165
Phe Lys Ser Ile Tyr Met Ala Lys Lys Pro Val Gln Leu Pro Gly Tyr
                                185
Tyr Tyr Val Asp Ser Lys Leu Asp Ile Thr Ser His Asn Glu Asp Tyr
                            200
Thr Ile Val Glu Gln Tyr Glu Arg Thr Glu Gly Arg His His Leu Phe
                        215
Leu
225
<210> 13
<211> 675
<212> DNA
<213> Artificial Sequence
<220>
<223> non-aggregating mutant
<400> 13
atggcetect cegagaacgt catcacegag tteatgeget teaaggtgeg catggaggge 60
acceptgaace gccacegagtt ceaegatcegae geceaegegee aggeceecc ctacegaegee 120
cacaacaccg tgaagetgaa ggtgaccaag ggcggccccc tgcccttcgc ctgggacatc 180
ctgtccccc agttccagta cggctccaag gtgtacgtga agcaccccgc cgacatcccc 240
gactacaaga agctgtcctt ccccgagggc ttcaagtggg agcgcgtgat gaacttcgag 300
gacggcggcg tggcgaccgt gacccaggac tcctccctgc aggacggctg cttcatctac 360
aaggtgaagt tcatcggcgt gaacttcccc tccgacggcc ccgtgatgca gaagaagacc 420
atgggctggg aggcctccac cgagcgcctg tacccccgcg acggcgtgct gaagggcgag 480
acccacaagg ccctgaagct gaaggacggc ggccactacc tggtggagtt caagtccatc 540
tacatggcca agaagcccgt gcagctgccc ggctactact acgtggacgc caagctggac 600
atcacctccc acaacgagga ctacaccatc gtggagcagt acgagcgcac cgagggccgc 660
                                                                   675
caccacctgt tcctg
<210> 14
<211> 678
<212> DNA
<213> Artificial Sequence
<220>
<223> non-aggregating mutant
<400> 14
atggeeteet cegagaacgt cateacegag tteatgeget teaaggtgeg catggaggge 60
acceptgaacg gccacgagtt cgagatcgag ggcgagggcg agggccgccc ctacgagggc 120
```

```
cacaacaccg tgaagttgaa ggtgaccaaq qqcqqcccc tqcccttcqc ctqqqacatc 180
ctgtccccc agttccagta cggctccaag gtgtacgtga agcaccccgc cgacatcccc 240
gactacaaga agctgtcctt ccccgagggc ttcaagtggg agcgcgtgat gaacttcgag 300
gacggcggcg tggcgaccgt gacccaggac tcctccctgc aggacggctg cttcatctac 360
aaggtgaagt tcatcggcgt gaacttcccc tccgacggcc ccgtgatgca gaagaagacc 420
atgggctggg aggcctccac cgagcgcctg tacccccqcg acggcgtqct gaaqqqcqaq 480
atccacaagg ccctgaagct gaaggacggc ggccactacc tggtggagtt caaqtccatc 540
tacatggcca agaagcccgt gcagctgccc ggctactact acgtggacac caagctggac 600
atcacctccc acaacgagga ctacaccatc gtggagcagt acgagcgcac cgagggccgc 660
caccacctgt tcctgtaa
<210> 15
<211> 705
<212> DNA
<213> Artificial Sequence
<220>
<223> non-aggregating mutant
<400> 15
ggatccgctc agtcagagca cggtctaaca gaagaaatga caatgaaata ccgtatggaa 60
gggtgcgtcg atggacataa atttgtgatc acgggagagg gcattggata tccgttcaaa 120
gggaaacagg ctattaatct gtgtgtggtc gaaggtggac cattgccatt tgccgaagac 180
atattgtcag ctgcctttat gtacggaaac agggttttca ctgaatatcc tcaagacata 240
gttgactatt tcaagaactc gtgtcctgct ggatatacat gggacaggtc ttttctcttt .300
gaggatggag cagtttgcat atgtaatgca gatataacag tgagtgttga agaaaactgc 360
atgtatcatg agtccaaatt ctatggagtg aattttcctg ctgatggacc tgtgatgaaa 420
aagatgacag ataactggga gccatcctgc gagaagatca taccaqtacc taaqcaqqqq .480
atattgaaag gggatgtete catgtacete ettetgaagg atggtgggeg tttaeggtge 540
caattcgaca cagtttacaa agcaaagtct gtgccaagaa agatgccgga ctggcacttc 600
atccagcata ageteaceeg tgaagacege agegatgeta agaatcagaa atggeatetg 660
acagaacatg ctattgcatc cggatctgca ttgccctgaa agctt
                                                                   705
<210> 16
<211> 230
<212> PRT
<213> Artificial Sequence
<220>
<223> non-aggregating mutant
<400> 16
Ala His Ser Glu His Gly Leu Thr Glu Glu Met Thr Met Lys Tyr His
                                    10
Met Glu Gly Cys Val Asn Gly His Lys Phe Val Ile Thr Gly Glu Gly
            20
                                25
Ile Gly Tyr Pro Phe Lys Gly Lys Gln Thr Ile Asn Leu Cys Val Ile
Glu Gly Gly Pro Leu Pro Phe Ser Glu Asp Ile Leu Ser Ala Gly Phe
Lys Tyr Gly Asp Arg Ile Phe Thr Glu Tyr Pro Gln Asp Ile Val Asp
```

```
65
                     70
                                          75
 Tyr Phe Lys Asn Ser Cys Pro Ala Gly Tyr Thr Trp Gly Arg Ser Phe
                 85
                                      90
 Leu Phe Glu Asp Gly Ala Val Cys Ile Cys Asn Val Asp Ile Thr Val
 Ser Val Lys Glu Asn Cys Ile Tyr His Lys Ser Ile Phe Asn Gly Val
                             120
 Asn Phe Pro Ala Asp Gly Pro Val Met Lys Lys Met Thr Thr Asn Trp
                         135
                                              140
 Glu Ala Ser Cys Glu Lys Ile Met Pro Val Pro Lys Gln Gly Ile Leu
 145
                     150
                                          155
 Lys Gly Asp Val Ser Met Tyr Leu Leu Leu Lys Asp Gly Gly Arg Tyr
                 165
                                      170
 Arg Cys Gln Phe Asp Thr Val Tyr Lys Ala Lys Ser Val Pro Ser Lys
                                 185
 Met Pro Glu Trp His Phe Ile Gln His Lys Leu Leu Arg Glu Asp Arg
                             200
 Ser Asp Ala Lys Asn Gln Lys Trp Gln Leu Thr Glu His Ala Ile Ala
                         215
 Phe Pro Ser Ala Leu Ala
 225
                     230
<210> 17
 <211> 705
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> non-aggregating mutant
 <400> 17
 ggatccgccc acagcgagca cggcctgacc gaggagatga ccatgaagta ccacatggag 60
 ggctgcgtga acggccacaa gttcgtgatc accggcgagg gcatcggcta ccccttcaag 120
 ggcaagcaga ccatcaacct gtgcgtgatc gagggcggcc ccctgccctt cagcgaggac 180
 atcctgagcg ccggcttcaa gtacggcgac cggatcttca ccgagtaccc ccaggacatc 240
 gtggactact tcaagaacag ctgccccgcc ggctacacct ggggccggag cttcctgttc 300
 gaggacggcg ccgtgtgcat ctgtaacgtg gacatcaccg tgagcgtgaa ggagaactgc 360
 atctaccaca agagcatctt caacggcgtg aacttccccq ccqacqqccc cqtqatqaaq 420
 aagatgacca ccaactggga ggccagctgc gagaagatca tgcccgtgcc taagcagggc 480
 atcctgaagg gcgacgtgag catgtacctg ctgctgaagg acggcggccg gtaccggtgc 540
 cagttcgaca ccgtgtacaa ggccaagagc gtgcccagca agatgcccga gtggcacttc 600
 atccagcaca agctgctgcg ggaggaccgg agcgacgcca agaaccagaa gtggcagctg 660
 accgagcacg ccatcgcctt ccccagcgcc ctggcctgaa agctt
                                                                    705
 <210> 18
 <211> 230
 <212> PRT
 <213> Artificial Sequence
 <220>
```

```
<400> 18
Ala His Ser Glu His Gly Leu Thr Glu Glu Met Thr Met Lys Tyr His
Met Glu Gly Cys Val Asn Gly His Lys Phe Val Ile Thr Gly Glu Gly
                                 25
Ile Gly Tyr Pro Phe Lys Gly Lys Gln Thr Ile Asn Leu Cys Val Ile
                             40
Glu Gly Gly Pro Leu Pro Phe Ser Glu Asp Ile Leu Ser Ala Gly Phe
Lys Tyr Gly Asp Arg Ile Phe Thr Glu Tyr Pro Gln Asp Ile Val Asp
                    70
Tyr Phe Lys Asn Ser Cys Pro Ala Gly Tyr Thr Trp Gly Arg Ser Phe
Leu Phe Glu Asp Gly Ala Val Cys Ile Cys Asn Val Asp Ile Thr Val
            100
                                105
Ser Val Lys Glu Asn Cys Ile Tyr His Lys Ser Ile Phe Asn Gly Val
                             120
                                                 125
Asn Phe Pro Ala Asp Gly Pro Val Met Lys Lys Met Thr Thr Asn Trp
                        135
Glu Ala Ser Cys Glu Lys Ile Met Pro Val Pro Lys Gln Gly Ile Leu
                    150
                                        155
Lys Gly Asp Val Ser Met Tyr Leu Leu Leu Lys Asp Gly Gly Arg Tyr
                                     170
Arg Cys Gln Phe Asp Thr Val Tyr Lys Ala Lys Ser Val Pro Ser Lys
                                185
Met Pro Glu Trp His Phe Ile Gln His Lys Leu Leu Arg Glu Asp Arg
                            200
Ser Asp Ala Lys Asn Gln Lys Trp Gln Leu Thr Glu His Ala Ile Ala
                        215
                                            220
Phe Pro Ser Ala Leu Ala
225
                    230
<210> 19
<211> 690
<212> DNA
<213> Artificial Sequence
<220>
<223> non-aggregating mutant
<400> 19
atggccctgt ccaacgagtt catcggcgac gacatgaaga tgacctacca catggacggc 60
tgcgtgaacg gccactactt caccgtgaag ggcgagggca gcggcaagcc ctacgagggc 120
acccagacet ccacettcaa ggtgaccatg gccaacggcg gccccctggc cttctccttc 180
gacateetgt ecacegtgtt catgtaegge aacegetget teacegeeta ecceaceage 240
atgcccgact acttcaagca ggccttcccc gacggcatgt cctacgagag aaccttcacc 300
tacgaggacg gcggcgtggc caccgccagc tgggagatca gcctgaaggg caactgcttc 360
```

gagcacaagt ccaccttcca cggcgtgaac ttccccgccg acggccccgt gatggccaag 420

```
aagaccaccg gctgggaccc ctccttcgag aagatgaccg tgtgcgacgg catcttgaag 480
 ggcgacgtga ccgccttcct gatgctgcag ggcggcggca actacagatg ccagttccac 540
 acctcctaca agaccaagaa gcccgtgacc atgcccccca accacgtggt ggagcaccgc 600
 ategecagaa eegaeetgga caagggegge aacagegtge agetgaeega geaegeegtg 660
gcccacatca cctccgtggt gcccttctga
 <210> 20
 <211> 229
 <212> PRT
<213> Artificial Sequence
<220>
<223> non-aggregating mutant
<400> 20
Met Ala Leu Ser Asn Glu Phe Ile Gly Asp Asp Met Lys Met Thr Tyr
His Met Asp Gly Cys Val Asn Gly His Tyr Phe Thr Val Lys Gly Glu
                                 25
Gly Ser Gly Lys Pro Tyr Glu Gly Thr Gln Thr Ser Thr Phe Lys Val
                             40
Thr Met Ala Asn Gly Gly Pro Leu Ala Phe Ser Phe Asp Ile Leu Ser
                        55
Thr Val Phe Met Tyr Gly Asn Arg Cys Phe Thr Ala Tyr Pro Thr Ser
Met Pro Asp Tyr Phe Lys Gln Ala Phe Pro Asp Gly Met Ser Tyr Glu
                                     90
Arg Thr Phe Thr Tyr Glu Asp Gly Gly Val Ala Thr Ala Ser Trp Glu
                                105
Ile Ser Leu Lys Gly Asn Cys Phe Glu His Lys Ser Thr Phe His Gly
                            120
Val Asn Phe Pro Ala Asp Gly Pro Val Met Ala Lys Lys Thr Thr Gly
                        135
                                             140
Trp Asp Pro Ser Phe Glu Lys Met Thr Val Cys Asp Gly Ile Leu Lys
                    150
                                         155
Gly Asp Val Thr Ala Phe Leu Met Leu Gln Gly Gly Asn Tyr Arg
                                    170
Cys Gln Phe His Thr Ser Tyr Lys Thr Lys Lys Pro Val Thr Met Pro
Pro Asn His Val Val Glu His Arg Ile Ala Arg Thr Asp Leu Asp Lys
                            200
Gly Gly Asn Ser Val Gln Leu Thr Glu His Ala Val Ala His Ile Thr
                        215
                                            220
Ser Val Val Pro Phe
225
<210> 21
<211> 707
<212> DNA
<213> Artificial Sequence
```

Tyr Arg Ser Lys Lys Pro Ala Ser Ala Leu Lys Met Pro Gly Phe His 185 Phe Glu Asp His Arg Ile Glu Ile Leu Glu Glu Val Glu Lys Gly Lys

```
195
                            200
                                               205
Cys Tyr Lys Gln Tyr Glu Ala Ala Val Gly Arg Tyr Cys Asp Ala Ala
                        215
                                           220
Pro Ser Lys Leu Gly His Asn
225
<210> 23
<211> 654
<212> DNA
<213> Artificial Sequence
<220>
<223> non-aggregating mutant
<400> 23
gagggcaccg tgaacggcca ctacttcaag tgcaccggca agggcgaggg caaccccctc 60
gagggcaccc aggagatgaa gatcgaggtg atcgagggcg gccccctgcc cttcgccttc 120
cacateetgt ecaceteetg catgtaegge tecaaggeet teateaagta egtgteegge 180
atccccgact acttcaagca gtccctcccc gagggcttca cctgggagcg caccaccacc 240
tacgaggacg gcggcttcct gaccgcccac caggacacct ccctggacgg cgactgcctg 300
gtgtacaagg tgaagateet gggcaacaae tteecegeeg acggeecegt gatgcagaac 360
aaggccggcc gctgggagcc ctccaccgag atcgtgtacg aggtggacgg cgtgctgcgc 420
accacctacc gctccaagaa gcccgcctcc gccctgaaga tgcccggctt ccacttcgag 540
gaccaccgca tcgagatcct ggaggaggtg gagaagggca agtgctacaa gcagtacgag 600
gccgccgtgg gccgctactg cgacgccgcc ccctccaagc tgggccacaa ctga
<210> 24
<211> 232
<212> PRT
<213> Artificial Sequence
<220>
<223> non-aggregating mutant
<400> 24
Met Ala Ser Leu Leu Thr Glu Thr Met Pro Phe Arg Thr Thr Ile Glu
Gly Thr Val Asn Gly His Tyr Phe Lys Cys Thr Gly Lys Gly Glu Gly
                               25
Asn Pro Leu Glu Gly Thr Gln Glu Met Lys Ile Glu Val Ile Glu Gly
                           40
Gly Pro Leu Pro Phe Ala Phe His Ile Leu Ser Thr Ser Cys Met Tyr
                       55
Gly Ser Lys Ala Phe Ile Lys Tyr Val Ser Gly Ile Pro Asp Tyr Phe
Lys Gln Ser Leu Pro Glu Gly Phe Thr Trp Glu Arg Thr Thr Tyr
                                  90
Glu Asp Gly Gly Phe Leu Thr Ala His Gln Asp Thr Ser Leu Asp Gly
```

105

```
Asp Cys Leu Val Tyr Lys Val Lys Ile Leu Gly Asn Asn Phe Pro Ala
                            120
        115
                                                125
Asp Gly Pro Val Met Gln Asn Lys Ala Gly Arg Trp Glu Pro Ser Thr
                        135
                                            140
Glu Ile Val Tyr Glu Val Asp Gly Val Leu Arg Gly Gln Ser Ser Met
                    150
                                        155
Ala Leu Glu Cys Pro Gly Gly Arg His Leu Thr Cys His Leu His Thr
                                    170
Thr Tyr Arg Ser Lys Lys Pro Ala Ser Ala Leu Lys Met Pro Gly Phe
His Phe Glu Asp His Arg Ile Glu Ile Leu Glu Glu Val Glu Lys Gly
                            200
Lys Cys Tyr Lys Gln Tyr Glu Ala Ala Val Gly Arg Tyr Cys Asp Ala
                        215
Ala Pro Ser Lys Leu Gly His Asn
                    230
<210> 25
<211> 26
<212> PRT
<213> Artificial Sequence
<223> non-aggregating mutant fragment
<400> 25
Met Arg Ser Ser Lys Asn Val Ile Lys Glu Phe Met Arg Phe Lys Val
                5
Arg Met Glu Gly Thr Val Asn Gly His Glu
            20
<210> 26
<211> 26
<212> PRT
<213> Artificial Sequence
<220>
<223> non-aggregating mutant fragment
Met Ser Cys Ser Lys Asn Val Ile Lys Glu Phe Met Arg Phe Gln Val
                5
Arg Met Glu Gly Thr Val Asn Gly His Glu
            20
```

<210> 27 <211> 26 <212> PRT

```
<213> Artificial Sequence
<220>
<223> non-aggregating mutant fragment
<400> 27
Met Ala Gln Ser Lys His Gly Leu Thr Lys Glu Met Thr Met Lys Tyr
Arg Met Glu Gly Cys Val Asp Gly His Lys
            20
<210> 28
<211> 26
<212> PRT
<213> Artificial Sequence
<220>
<223> non-aggregating mutant fragment
<400> 28
Met Ala His Ser Lys His Gly Leu Lys Glu Glu Met Thr Met Lys Tyr
                 5
His Met Glu Gly Cys Val Asn Gly His Lys
            20
<210> 29
<211> 26
<212> PRT
<213> Artificial Sequence
<220>
<223> non-aggregating mutant fragment
<400> 29
Met Ala Leu Ser Asn Lys Phe Ile Gly Asp Asp Met Lys Met Thr Tyr
                 5
His Met Asp Gly Cys Val Asn Gly His Tyr
            20
<210> 30
<211> 23
<212> PRT
<213> Artificial Sequence
<220>
<223> non-aggregating mutant fragment
```

<400> 30

Met Ala Ser Phe Leu Lys Lys Thr Met Pro Phe Lys Thr Thr Ile Glu

1 5 10 15

Gly Thr Val Asn Gly His Tyr
20